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U.S. DEPARTMENT OF COMMERCE
PATENT AND TRADEMARK OFFICE

TRANSMITTAL LETTER		Docket Number: 1247/9	
Application Number 726,178	Filing Date 4/23/85	Examiner	Art Unit
Patent Number 4,692,435	Issue Date September 8, 1987		
Invention Title Mucopolysaccharide Composition Having a Regulatory Action on Coagulation, Medicament Containing Same and Process of Preparation		Inventor(s) Lormeau et al.	

Address to:
Commissioner of Patents and Trademarks
Washington D.C. 20231
Box Pat. Ext.

SIR:

Please find enclosed an Amended Application for Extension of Patent Term Under 35 U.S.C. 156 which is being filed in connection with the above-referenced patent.

This paper amends section 8 of the original application to specifically state that a receipt for maintenance fee payment is provided as Exhibit C. It further amends section 10 to include both the date that the NDA was initially submitted (July 26, 1991) and the effective date of the NDA submission (December 31, 1991).

The amended application also corrects the calculation of the length of extension of the patent term claimed by the applicant in section 12 of the original application. In particular, the calculations in subparagraphs (h), (j), (l), (m) and (n) have been amended on page 10. The amended section 12 also claims, in the alternative, the length of extension computed by the Federal Drug Administration and published at 58 Fed. Reg. 62,356 (1993).

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner of Patents and Trademarks, Washington, D. C. 20231, on

Date 12-21-93 Atty's Reg. # 25,054

Atty's Signature Albert J. Breneisen

KENYON & KENYON
ALBERT J. BRENEISEN

The applicant wishes to bring to the attention of the Patent Office that it will seek a redetermination by the Federal Drug Administration ("FDA") of the length of extension. In particular, the length of the testing period should be calculated from the effective date of the IND up to the date the NDA application was initially submitted (July 26, 1991) and not up to the date the NDA application was deemed effective by the FDA (December 31, 1991).

Respectfully submitted,

Dated: December 20, 1993

Albert J. Breneisen
(Reg. No. 25,054)

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Please charge any fees to Deposit Account No.11-0600.

U.S. DEPARTMENT OF COMMERCE
PATENT AND TRADEMARK OFFICE

AMENDED APPLICATION FOR EXTENSION OF PATENT TERM UNDER 35 U.S.C. 156

Docket Number: 1247/9

Application Number	Filing Date	Examiner	Art Unit
726,178	4/23/85		
Patent Number	**Issue Date**		
4,692,435	September 8, 1987		

Invention Title: Mucopolysaccharide Composition Having a Regulatory Action on Coagulation, Medicament Containing Same and Process of Preparation

Inventor(s): Lormeau et al.

Address to:
Commissioner of Patents and Trademarks
Washington D.C. 20231
Box Pat. Ext.

I Hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner of Patents and Trademarks, Washington, D. C. 20231, on

Date 12-21-93 Atty's Reg. # 25,054

Atty's Signature Albert J. Breneman

KENYON & KENYON
ATTORNEYS AT LAW

Choay, S.A., assignee and owner of the entire 100% interest in U.S. patent 4,692,435 (the "'435 patent") submits this request for patent term extension for the '435 patent.

(1) The approved product is LOVENOX® enoxaparin, a low molecular weight heparin product, containing a mixture of lower molecular weight fractions in the range of about 2,000 to about 4,000 daltons with higher molecular weight fractions of a molecular weight in the range of about 4,000 to about 10,000 daltons as determined by gel permeation chromatography.

(2) Regulatory review of LOVENOX® enoxaparin occurred under 21 U.S.C. § 355.

(3) the LOVENOX® product received permission for commercial marketing under 21 U.S.C. § 355 on March 29, 1993.

(4) The only active ingredient in the LOVENOX® product is enoxaparin. Enoxaparin has not been previously approved for commercial marketing or use under the Federal Food, Drug and Cosmetic Act, the Public Health Service Act, or the Virus-Serum-Toxin Act.

(5) This application is being submitted by the owner of the '435 patent, Choay S.A., within the sixty day period permitted for submission pursuant to 37 CFR § 1.720(f). The last day on which the application could be submitted is May 28, 1993.

(6) The patent for which an extension is being sought is U.S. 4,692,435, issued September 8, 1987. The inventors were Jean-Claude Lormeau, Jean Goulay, and Jean Choay. The '435 patent currently expires December 4, 2001.

(7) A copy of the '435 patent is attached hereto as Exhibit A.

(8) A copy of a terminal disclaimer, disclaiming the terminal portion of the '435 patent is attached hereto as Exhibit B. No certificates of correction or reexamination certificates have been issued. A copy of a receipt for maintenance fee payment is provided as Exhibit C.

(9) The '435 patent claims the approved product, methods of using the approved product, and methods of making the approved product. The applicable patent claims and the manner in which each applicable claim reads on the approved product or method of using the approved product follows:

> Claim 18. Heparinic mucopolysaccharide fractions having constituents of a molecular weight not in excess of about 10,000 daltons, which fractions have (1) a mixture of lower molecular weight fractions in the range of about 2,000 to about 4,000 daltons with higher molecular weight fractions of a molecular weight in the range of about 4,000 to about 10,000 daltons, (2) a Yin-Wessler of at least 40, and (3) a ratio of Yin-Wessler to USP titer in the range of 3 to 5, which mixture of fractions have improved antithrombotic activity in vivo which is higher than that of heparin and a whole anticoagulation activity lower than that of heparin, and the physiologically acceptable salts thereof.

LOVENOX® enoxaparin contains heparinic mucopolysaccharide fractions having

(a) The Lovenox® product package insert indicates that, at minimum, 68% of the LOVENOX® mucopolysaccharides have molecular weights between 2000 and 8000 daltons; no more than 15% have molecular weight greater than 8000 daltons, and no more than 20% have molecular weights less than 2,000 daltons. A study on the LOVENOX® product by Choay indicated that 90% of the mucopolysaccharides had molecular weights between 1900 and 8500 daltons, and fewer than 1% had molecular weights greater than 11,000 daltons, or less than 1600 daltons, as measured by gel permeation chromatography;

(b) A study on the LOVENOX® product by Choay indicated that

(i) roughly half of the mucopolysaccharides had molecular weight between 10333 and 4096 daltons, and roughly half have molecular weight between 4096 and 2050 daltons;

(ii) it exhibitited a Yin-Wessler of at least 40, namely approximately 240-250 U/mg;

(iii) a ratio of Yin-Wessler to USP titer in the range of 3 to 5, namely about 4.36;

(c) The LOVENOX® product has improved antithrombotic activity in vivo which is higher than that of heparin and a whole anticoagulation activity lower than that of heparin.

(d) The LOVENOX® mucopolysaccharide fractions are sodium salts.

Claim 19. The heparinic mucopolysaccharide fractions of claim 18 wherein the lower molecular weight fractions are free of nucleic acids.

LOVENOX® enoxaparin is substantially free of nucleic acids.

Claim 21. The heparinic mucopolysaccharides of claim 18 wherein the molecular weight is not in excess of about 8,000 daltons.

See the comment above on the molecular weight of LOVENOX® mucopolysaccharides.

Claim 31. The heparinic mucopolysaccharides of claim 18 wherein fractions have a molecular weight range of about 2,000 to about 8,000.

See the comment above on the molecular weight of LOVENOX® mucopolysaccharides.

Claim 32. The heparinic mucopolysaccharide fractions of claim 19 which are soluble in an aqueous-alcoholic medium, and insoluble in pure alcohol.

The LOVENOX® enoxaparin heparinic mucopolysaccharide fractions are soluble in an aqueous-alcoholic medium, and insoluble in pure alcohol.

Claim 11. A therapeutic composition for controlling thrombosis and decreasing hemorrhaging and of blood hypercoagulation risks which comprises a therapeutically acceptable carrier and heparinic mucopolysaccharide fractions having constituents of a molecular weight not in excess of about 10,000 daltons, which fractions have (1) a mixture of lower molecular weight fractions in the range of about 2,000 to about 4,000 daltons with higher molecular weight fractions of a molecular weight in the range of about 4,000 to about 10,000 daltons, (2) a Yin-Wessler of at least 40, and (3) a ratio of Yin-Wessler to USP titer in the range of 3 to 5, and the physiologically acceptable

salts thereof, which mixture of fractions have improved antithrombotic activity in vivo which is higher than that of heparin and a whole anticoagulation activity lower and slower than that of heparin.

The LOVENOX® product is a therapeutic composition for controlling thrombosis and decreasing hemorrhaging and of blood hypercoagulation risks. It contains a therapeutically acceptable carrier. The composition of the mucopolysaccharide fractions is described above with respect to claim 18.

Claim 12. The therapeutic composition of claim 11 which is a solution.

The LOVENOX® product is marketed as a solution.

Claim 13. The therapeutic composition of claim 12 wherein the heparinic mucopolysaccharides fractions are in solution in a concentration of about 1,000 to 100,000 Yin-Wessler units per ml.

The LOVENOX® product is marketed in solution. Choay S.A. has determined that the solution has a concentration of roughly 25,000 Yin-Wessler units per mL.

Claim 14. The therapeutic composition of claim 13 which is a solution of the mucopolysaccharides in a concentration of about 5,000 to about 50,000 Yin-Wessler units per ml.

The LOVENOX® product is marketed in solution. Choay S.A. has determined that the solution has a concentration of roughly 25,000 Yin-Wessler units per mL.

Claim 15. The solution of claim 12 which is apyrogenic.

The LOVENOX® product is apyrogenic.

Claim 16. The solution of claim 15 which is sterile.

The LOVENOX® product is sterile.

Claim 4. A therapeutic method for controlling thrombosis and decreasing blood hypercoagulation and hemorrhaging risks in a

patient which comprises administering to the patient in an antithrombotic effective amount, a composition which comprises a therapeutically acceptable carrier and heparinic mucopolysaccharide fractions having constituents of a molecular weight not in excess of about 10,000 daltons, which fractions have (1) a mixture of lower molecular weight fractions in the range of about 2,000 to about 4,000 daltons with higher molecular weight fractions of a molecular weight in the range of about 4,000 to about 10,000 daltons, (2) a Yin-Wessler of at least 40, and (3) a ratio of Yin-Wessler to USP titer in the range of 3 to 5, and the physiologically acceptable salts thereof, which mixture of fractions have improved antithrombotic activity in vivo which is higher than that of heparin and a whole anticoagulation activity lower than that of heparin, and said method controlling thrombosis by selectively inhibiting coagulation factor Xa while also having a whole anticoagulation effect which is slower and lower than that of heparin.

The LOVENOX® therapeutic composition has been approved by the FDA for use in a method for prevention of deep vein thrombosis, which may lead to pulmonary embolism following hip replacement surgery, via injection of LOVENOX® solution. The composition has been described above under claim 18.

Claim 5. The method of claim 4 wherein the administration is by injection or infusion to the patient.

The LOVENOX® product has been approved by the FDA for administration by injection.

Claim 6. The method of claim 5 wherein the administration by injection is sub-cutaneous.

LOVENOX® has been approved by the FDA for administration by injection. It is not indicated for intramuscular administration. It may be administered sub-cutanaceously.

Claim 7. The method of claim 6 wherein the dosage administered sub-cutaneously is from about 1,000 to about 25,000 Yin-Wessler units per ml.

The LOVENOX® product is marketed in solution. Choay S.A. has determined that the concentration is roughly 25,000 Yin-Wessler units per mL.

Claim 47. The therapeutic method of claim 4 wherein the patient is exposed to risks of hypercoagulatability.

LOVENOX® enoxaparin is indicated for patients who are exposed to risks of hypercoagulatability.

> Claim 33. A therapeutic composition which presents less risks than heparin of blood hypercoagulation and of a host hemorrhaging, which composition has improved antithrombotic activity (anti-Xa activity) and improved selectivity with respect to anti-Xa activity than heparin in vivo and a lower and slower anticoagulation activity than heparin, and which composition comprises a therapeutically acceptable carrier and an antithrombotic effective amount of heparinic mucopolysaccharide fractions having constituents of a molecular weight not in excess of about 10,000 daltons, which fractions have (1) a mixture of lower molecular weight fractions in the range of about 2,000 to about 4,000 daltons with higher molecular weight fractions of a molecular weight in the range of about 4,000 to about 10,000 daltons, (2) a Yin-Wessler of at least 40, and (3) a ratio of Yin-Wessler to USP titer in the range of 3 to 5, which mixture of fractions have improved antithrombotic activity in vivo which is higher than that of heparin and a whole anticoagulation activity lower than that of heparin, and the physiologically acceptable salts thereof.

The LOVENOX® product is a therapeutic composition which presents less risks than heparin of blood hypercoagulation and of a host hemorrhaging. The composition and properties of LOVENOX® are discussed above with respect to claim 18.

> Claim 35. The therapeutic composition of claim 33 in which the molecular weight of the heparinic mucopolysaccharides is not in excess of about 8,000 daltons.

See comment (a) to claim 18 for the molecular weight distribution of LOVENOX® enoxaparin.

(10) The relevant dates and information pursuant to 35 USC 156(g) in order to enable the Secretary of Health and Human Services to determine the applicable regulatory review period is:

IND number:	31532
IND effective date:	May 19, 1988
NDA number	20-164
NDA submission date:	July 26, 1991
NDA effective date:	December 31, 1991
NDA approval date:	March 29, 1993

(11) The LOVENOX® NDA was approved by the FDA on an IND and NDA filed by Rhone-Poulenc Rorer Pharmaceuticals, Inc. ("RPRP"), the licensee of the '435 patent. As a brief description of the significant activities undertaken by Rhone-Poulenc Rorer Pharmaceuticals, Inc., during the applicable regulatory review period with respect to the approved product and the significant dates applicable to such activities, attached hereto as Exhibit D is a brief chronology of the communications with the FDA during the regulatory review period ending with approval on March 29, 1993.

(12) In the opinion of the applicant, the '435 patent is eligible for patent term extension under 35 USC 156 because .

(a) 35 U.S.C 156(a)
The '435 patent claims a product, and a method of using a product.

(b) 35 U.S.C 156(a)(1)
The term of the '435 patent has not expired before submission of this application.

(c) 35 U.S.C. 156(a)(2)
The term of the '435 patent has never been extended.

(d) 35 U.S.C. 156(a)(3)
The application for extension is submitted by Choay S.A., the owner of record in accordance with the requirement of 35 U.S.C. 156(d) and rules of the U.S. Patent and Trademark Office.

(e) 35 U.S.C. 156(a)(4)
The LOVENOX® product has been subjected to a regulatory review period before its commercial marketing or use.

(f) 35 U.S.C. 156(a)(5)(A)
The commercial marketing or use of the LOVENOX® product, after the regulatory review period is the first permitted commercial marketing or use of LOVENOX® product under the provision of the Federal Food Drug and Cosmetic Act (21 U.S.C. 355) under which such regulatory review period occurred.

(g) 35 U.S.C. 156(c)(4)
No other patent has been extended for the same regulatory review period for the LOVENOX® product.

The length of extension of the patent term of the '435 patent claimed by applicant is 1,195 days, until March 13, 2005. The length of the extension was determined pursuant to 37 C.F.R. 1.775 as follows:

(a) 1164 The number of days in the period beginning on the date an exemption under subsection (i) of section 505 or subsection (d) of section 507 of the Federal Food Drug and Cosmetic Act became effective for the approved product (May 19, 1988) and ending on the date the application was initially submitted for such product under those sections or under section 351 of the Public Health Service Act (July 26, 1991); (37 C.F.R. 1.775(c)(1))

(b)	613	The number of days in the period beginning on the date the application was initially submitted for the approved product under section 351 of the Public Health Service Act, subsection (b) of section 505 or section (507) of the Federal Food, Drug, and Cosmetic Act (July 26, 1991) and ending on the date such application was approved under such section (March 29, 1993). (37 C.F.R. 1.775(c)(2))
(c)	1777	The sum of (a) and (b). This is the regulatory review period. (37 C.F.R. 1.775(c))
(d)	0	the number of days in the regulatory review period which were on and before the '435 patent issued (September 8, 1987). (37 C.F.R. 1.775(d)(1)(i))
(e)	0	the number of days in the regulatory review period during which it is determined under 35 U.S.C 56(d)(2)(B) by the Secretary of Health and Human Services that applicant did not act with due diligence.[1] (37 C.F.R. 1.775(d)(1)(ii))
(f)	0	the sum of (d) and (e).
(g)	1777	(c) - (f). (37 C.F.R. 1.775(d)(1)(ii))
(h)	1195	1/2 of (a) + (b). (37 C.F.R. 1.775(d)(1)(iii))
(i)	12/04/2001	The original term of the '435 patent, shortened by any terminal disclaimer.
(j)	03/13/2005	The original term of the patent as shortened by any terminal disclaimer plus the number of days in (h). (37 C.F.R. 1.775(d)(2))
(k)	03/29/2007	The date of approval of the application under section 351 of the Public Health Service Act, or subsection (b) of section 505 or section 507 of the Federal Food, Drug and Cosmetic Act plus 14 years. (37 C.F.R. 1.775(d)(3))
(l)	03/13/2005	The earlier of (j) and (k). (37 C.F.R. 1.775(d)(4))
(m)	12/04/2006	(i) plus 5 years. (37 C.F.R. 1.775(d)(5)(i))
(n)	03/13/2005	The earlier of (l) and (m). (37 C.F.R. 1.775(d)(5)(ii))

1. There has been no such determination. To the best of applicant's knowledge, RPRP was diligent during the regulatory review period.

Alternatively, the length of extension of the patent term of the '435 patent claimed by applicant is 1,116 days, until December 24, 2004, per the initial determination of the Food and Drug Administration as published at 58 Fed. Reg. 62,356 (1993). The length of the extension was determined as follows:

(a)	1322	The number of days in the period beginning on the date an exemption under subsection (i) of section 505 or subsection (d) of section 507 of the Federal Food Drug and Cosmetic Act became effective for the approved product (May 19, 1988) and ending on the date the application was initially submitted and effective for such product under those sections or under section 351 of the Public Health Service Act (December 31, 1991); (See 37 C.F.R. 1.775(c)(1); Determination of Regulatory Review Period for Purposes of Patent Extension; Lovenox®, 58 Fed. Reg. 62,356 (1993))
(b)	455	The number of days in the period beginning on the date the application was initially submitted and effective for the approved product under section 351 of the Public Health Service Act, subsection (b) of section 505 or section (507) of the Federal Food, Drug, and Cosmetic Act (December 31, 1991) and ending on the date such application was approved under such section (March 29, 1993). (See 37 C.F.R. 1.775(c)(2); Determination of Regulatory Review Period for Purposes of Patent Extension; Lovenox®, 58 Fed. Reg. 62,356 (1993))
(c)	1777	The sum of (a) and (b). This is the regulatory review period. (37 C.F.R. 1.775(c))
(d)	0	the number of days in the regulatory review period which were on and before the '435 patent issued (September 8, 1987). (37 C.F.R. 1.775(d)(1)(i))
(e)	0	the number of days in the regulatory review period during which it is determined under 35 U.S.C 56(d)(2)(B) by the Secretary of Health and Human Services that applicant did not act with due diligence.[2] (37 C.F.R. 1.775(d)(1)(ii))
(f)	0	the sum of (d) and (e).
(g)	1777	(c) - (f). (37 C.F.R. 1.775(d)(1)(ii))

2. There has been no such determination. To the best of applicant's knowledge, RPRP was diligent during the regulatory review period.

(h) 1116 1/2 of (a) + (b). (37 C.F.R. 1.775(d)(1)(iii))

(i) 12/04/2001 The original term of the '435 patent, shortened by any terminal disclaimer.

(j) 12/24/2004 The original term of the patent as shortened by any terminal disclaimer plus the number of days in (h). (37 C.F.R. 1.775(d)(2))

(k) 03/29/2007 The date of approval of the application under section 351 of the Public Health Service Act, or subsection (b) of section 505 or section 507 of the Federal Food, Drug and Cosmetic Act plus 14 years. (37 C.F.R. 1.775(d)(3))

(l) 12/24/2004 The earlier of (j) and (k). (37 C.F.R. 1.775(d)(4))

(m) 12/04/2006 (i) plus 5 years. (37 C.F.R. 1.775(d)(5)(i))

(n) 12/24/2004 The earlier of (l) and (m). (37 C.F.R. 1.775(d)(5)(ii))

(13) The applicant acknowledges a duty to disclose to the Commissioner of Patents and Trademarks and the Secretary of Health and Human Services or the Secretary of Agriculture any information which is material to the determination of entitlement to the extension sought.

(14) The proscribed fee for receiving and acting upon the original application for extension filed on May 24, 1993 pursuant to 37 C.F.R. 1.20(j) was charged to deposit account 11-0600. Please charge any additional fees for receiving and acting upont this amended application for patent term extension to deposit account 11-0600.

(15) Please address inquiries and correspondence to the undersigned.

(16) A triplicate of these application papers is submitted herewith.

(17) The following declaration is submitted herewith in compliance with the requirements of 37 C.F.R. § 1.740(b):

DECLARATION

The undersigned, Attorney for Choay, S.A., which is the applicant submitting this amended application for patent term extension of United States Patent No. 4,692,435 hereinabove referred to as the '435 patent, in compliance with the requirements of 37 C.F.R. § 1.740(b)(1), hereby avers as follows:

1. He is a patent attorney authorized to practice before the United States Patent and Trademark Office (Reg. No. 25,054) and he is authorized to represent Choay, S.A. in this amended application of patent term extension of the '435 patent and to transact all business in the United States Patent and Trademark Office in connection therewith;

2. He has reviewed and understands the contents of this amended application for patent term extension of the '435 patent;

3. He believes that the '435 patent is subject to patent term extension pursuant to the provisions of 37 C.F.R. § 1.710;

4. He believes that the extension of the length claimed in this amended application for patent term extension of the '435 patent is justified under 35 U.S.C. § 156 and the applicable regulations relating thereto; and

5. He believes that the '435 patent which is the subject of this amended application for patent term extension meets the conditions for patent term extension as set forth in 37 C.F.R. § 1.720.

Respectfully submitted,

Dated: December 20, 1993

Albert J. Breneisen
Reg. No. 25,054

Steven J. Lee
Reg. No. 31,272

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Choay, S.A.

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Exhibit A

United States Patent [19]

Lormeau et al.

[11] **Patent Number: 4,692,435**

[45] **Date of Patent: * Sep. 8, 1987**

[54] **MUCOPOLYSACCHARIDE COMPOSITION HAVING A REGULATORY ACTION ON COAGULATION, MEDICAMENT CONTAINING SAME AND PROCESS OF PREPARATION**

[75] Inventors: **Jean-Claude Lormeau**, Maromme-la-Maine; **Jean Goulay**, Oissel; **Jean Choay**, Paris, all of France

[73] Assignee: **Choay, S.A.**, Paris, France

[*] Notice: The portion of the term of this patent subsequent to Dec. 4, 2001 has been disclaimed.

[21] Appl. No.: **726,178**

[22] Filed: **Apr. 23, 1985**

Related U.S. Application Data

[63] Continuation of Ser. No. 204,505, Nov. 5, 1980, abandoned.

[30] **Foreign Application Priority Data**

Nov. 6, 1978 [FR] France 78 31357
Jul. 20, 1979 [FR] France 79 18873

[51] **Int. Cl.**[4] **A61K 31/725; C08B 37/10**
[52] **U.S. Cl.** **514/56; 536/21**
[58] **Field of Search** 536/21; 514/56

[56] **References Cited**

U.S. PATENT DOCUMENTS

4,168,377	9/1979	Choay et al.	424/183
4,175,182	11/1979	Schmer	536/21
4,281,108	7/1981	Fussi	424/183
4,303,651	12/1981	Lindahl et al.	424/183
4,315,923	2/1982	Takacs et al.	424/183
4,486,420	12/1984	Lormeau et al.	536/21

Primary Examiner—Johnnie R. Brown
Attorney, Agent, or Firm—Weiser & Stapler

[57] **ABSTRACT**

The invention pertains to a mucopolysaccharide fraction obtainable from heparin or from fractions including heparinic constituents of molecular weights from 2000 to 50,000, which has a Yin-Wessler titer which is high relative to the USP titer. It contains components whose molecular weights are less than 10,000, particularly oligosaccharides in the area of 2000–3000, comprising from 8 to 12, notably 10 monosaccharide units, among which glucosamine units whose primary positions are sulphated. The last mentioned oligosaccharides include one N-acetyl-glucosamine unit per two units of 2-O-sulphate iduronic acid and per two N-sulphate-glucosamine units, the other saccharide units being of a different nature and including distinct substituents.

48 Claims, 15 Drawing Figures

Exhibit B

2201479P/0257A/GW

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of	:	
JEAN CLAUDE LORMEAU ET AL	:	Group Art Unit: 125
Serial No 204,505	:	Examiner: J.R. Brown
Filed: November 6, 1980	:	703-557-3920
For a Patent for	:	
MUCOPOLYSACCHARIDE COMPOSITION HAVING A REGULATORY ACTION ON COAGULATION, MEDICAMENT CONTAINING IT AND PROCESS FOR PREPARING IT	:	January 31, 1984

TERMINAL DISCLAIMER UNDER 37 CFR 1.321(b)

Hon. Commissioner of Patents and Trademarks
Washington, D.C. 20231

Sir:

Choay S.A. of 48 Theophile Gautier 75782 Paris, Cedex 16 (France) the owner of record of application Serial No. 204,505 filed November 6, 1980 and of application Serial No. 301,611 filed September 14, 1981, as evidenced by the assignments recorded under Reel 3707 Frame 791 and Reel 3932 Frame 304, respectively, does hereby disclaim the terminal part of any patent granted on application Serial No. 204,505 which would extend beyond the expiration date any patent granted on application Serial No. 301,611, if the latter patent is granted first.

Choay S.A. hereby agrees any patents so granted on said application shall be enforceable only for and during such period that the legal title to said patents shall be the same.

This agreement shall run with any patent(s) granted on the above-said application and shall be binding upon the grantee, its successors or assigns.

CHOAY S.A.

by _____
Title: General Manager
P. Willaime

Exhibit C

UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D. C. 20231

75M1

GERARD J. WEISER, ESQ.
WEISER & STAPLER
SUITE 500
230 S. 15TH STREET
PHILADELPHIA, PENNSYLVANIA 19102

DATE MAILED
05/27/93

MAINTENANCE FEE STATEMENT

The data shown below is from the records of the Patent and Trademark Office. If the maintenance fees and any necessary surcharges have been timely paid for the patents listed below, the notation "PAID" will appear in column 10, "status" below.

If a maintenance fee payment is defective, the reason is indicated by code in column 10, "status" below. An explanation of the codes appears on the reverse of the Maintenance Fee Statement. TIMELY CORRECTION IS REQUIRED IN ORDER TO AVOID EXPIRATION OF THE PATENT. NOTE 37 CFR 1.377. THE PAYMENT(S) WILL BE ENTERED UPON RECEIPT OF ACCEPTABLE CORRECTION. IF PAYMENT OR CORRECTION IS SUBMITTED DURING THE GRACE PERIOD, A SURCHARGE IS ALSO REQUIRED. NOTE 37 CFR 1.20(k) and (l).

If the statement of small entity status is defective the reason is indicated below in column 10 for the related patent number. THE STATEMENT OF SMALL ENTITY STATUS WILL BE ENTERED UPON RECEIPT OF ACCEPTABLE CORRECTION.

ITM IBR	PATENT NUMBER	FEE CDE	FEE AMOUNT	SUR CHARGE	SERIAL NUMBER	PATENT DATE	FILE DATE	PAY YR	SML ENT	STAT
1	4,692,435	173	830	----	06/726,178	09/08/87	04/23/85	04	NO	PAID

Exhibit D

Rhône-Poulenc Rorer Central Research
Regulatory Affairs

APPLICATION CHRONOLOGY REPORT
Report Cover Page

Run Date: 05/05/93
User: ingres_prod

Selection Criteria

App Number: 20164

Rhône-Poulenc Rorer Central Research
Regulatory Affairs

APPLICATION CHRONOLOGY REPORT

Run Date: 05/05/93
App Num: 20164 Type: NDA Drug Code: RP 54563 Trade Name: LOVENOX INJECTION
Route of Admin.: SU Dosage Form: SOLUTION
Generic Name: enoxaparin 30 mg

COMM DATE	COMM TYPE	CONTENT Name/Description Details		Content Comments
26-JUL-91	ORIGINAL SUBMISSION	CLINICAL PRO#: INV NAME:	STUDY	
05-AUG-91	GENERAL CORRESP From FDA	OTHER	N/A	FDA ACKNOWLEDGED RECEIPT OF ORIGINAL NDA ON 29-JUL-91
20-SEP-91	GENERAL CORRESP From FDA	OTHER	N/A	FDA COMMENTS AFTER PRELIMINARY REVIEW OF ORIGINAL NDA SUBMISSION
15-OCT-91	GENERAL CORRESP To FDA	OTHER	N/A	CHANGE OF ADDRESS
01-NOV-91	AMENDMENT	OTHER	N/A	RESPONSE TO 20-SEP-91 FDA LETTER INDICATING REFUSAL TO FILE. INFO FOR DISCUSSION AT 13-NOV-91 INFORMAL CONFERENCE
15-NOV-91	MEETING MINUTES	OTHER	N/A	INFORMAL CONFERENCE TO DISCUSS THE REASONS THE NDA WAS NOT ACCEPTED FOR FILING
10-JAN-92	PHONE CALL	PRECLINICAL STUDY#: SPECIES: RTE. ADMIN: DURATION:	STUDY	MS. COLLIER RELAYED THE CSO'S QUESTIONS RE: THE RESUBMISSION
14-JAN-92	GENERAL CORRESP From FDA	OTHER	N/A	FDA ACKNOWLEDGED RECEIPT OF RESUBMITTED NDA ON 31-DEC-91. NEW DUE DATE IS 28-JUN-92
21-JAN-92	PHONE CALL	OTHER	N/A	CONSUMER SAFETY OFFICER REQUESTED ADDITIONAL COPIES OF CERTAIN VOLUMES
22-JAN-92	GENERAL CORRESP To FDA	OTHER	N/A	PROVIDED A NEW COPY OF THE SAS DATASETS OF EFFICACY & BLEEDING ASSESSMENT DATA FOR HIP REPLACEMENT SURGERY
24-JAN-92	GENERAL CORRESP To FDA	OTHER	N/A	PROVIDED DESK COPIES OF VOLUMES 77 AND 78

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COMM DATE	COMM TYPE	CONTENT Name/Description Details		Content Comments
28-JAN-92	GENERAL CORRESP To FDA	OTHER	N/A	PROVIDED FDA WITH A DESK COPY OF VOLUME 2.3
30-JAN-92	AMENDMENT	PRECLINICAL STUDY#: SPECIES: RTE. ADMIN: DURATION:	STUDY	RESPONSE TO THE QUESTIONS DR. AHMAD RAISED DURING HIS REVIEW OF NONCLINICAL DATA
04-FEB-92	PHONE CALL	CLINICAL PRO#: PAT NUM: 0 PAT INIT: PAT REACT: SRTYPE: Follow-up INV NAME:	SAFETY REPORT	CSO BRONNIE COLLIER STATED A SAFETY UPDATE WOULD NOT BE REQUIRED UNTIL THE APPLICATION APPROACHES APPROVABILITY
24-FEB-92	AMENDMENT	OTHER	N/A	FOUR APPENDICES CONTAINING INFO REQUESTED BY FDA
24-FEB-92	GENERAL CORRESP From FDA	CMC Dos Form/Potency: INJECTION	DRUG PRODUCT	
18-MAR-92	PHONE CALL	CMC Dos Form/Potency:	DRUG PRODUCT	FDA'S RESPONSE TO STABILITY DATA
19-MAR-92	AMENDMENT	LABEL/PRO MATERIAL FC NUM:	PACKAGE INSERT	RESPONSE TO 18-MAR-92 REQUEST FOR TWO DISKETTES OF PROPOSED PACKAGE INSERT
19-MAR-92	GENERAL CORRESP From FDA	CMC Dos Form/Potency:	DRUG PRODUCT	REQUEST FOR INFORMATION RE: STABILITY DATA FOR EXPIRATION DATING
26-MAR-92	AMENDMENT	CMC Dos Form/Potency:	DRUG PRODUCT	RESPONSE TO 24-FEB-92 REQUEST FOR FURTHER INFORMATION
31-MAR-92	AMENDMENT	OTHER	N/A	RESPONSE TO FDA REQUEST FOR INFORMATION RE: CLINICAL STUDY ENO 884
01-APR-92	AMENDMENT	CLINICAL PRO#: 526 INV NAME:	STUDY	RESPONSE TO 31-MAR-92 REQUEST FOR INFORMATION

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Route of Admin.: SU Dosage Form: SOLUTION
Generic Name: enoxaparin 30 mg

COMM DATE	COMM TYPE	CONTENT Name/Description Details		Content Comments
03-APR-92	GENERAL CORRESP From FDA	OTHER	N/A	31-MAR-92 SUBMISSION CONSIDERED MAJOR - EXTENDED DUE DATE TO 27-AUG-92
06-APR-92	AMENDMENT	CMC Dos Form/Potency:	DRUG PRODUCT	RESPONSE TO RECENT TELEPHONE REQUEST FOR SAMPLES OF SYRINGES AND BLISTER PACKAGES
08-APR-92	AMENDMENT	CMC Dos Form/Potency:	DRUG PRODUCT	RESPONSE TO 19-MAR-92 FDA REQUEST FOR ADDITIONAL STABILITY INFORMATION TO SUPPORT PROPOSED EXPIRATION DATING
08-APR-92	GENERAL CORRESP To FDA	OTHER	N/A	RESPONSE TO 02-APR-92 REQUEST FOR SPECIFIC INFO TO FACILITATE THE UPCOMING CLINICAL INVESTIGATOR INSPECTIONS IN CANADA
10-APR-92	GENERAL CORRESP To FDA	OTHER	N/A	ADDITIONAL INFO REQUESTED 02-APR-92 RE: CASE REPORT FORMS FOR EN0884 AT HAMILTON GENL HOSP & HENDERSON GENL HOSPITALS
17-APR-92	GENERAL CORRESP To FDA	OTHER	N/A	CONFIRMATION OF FDA INSPECTION DATE OF CLINICAL TRIAL EN0884 AT HENDERSON & HAMILTON HOSPITALS
21-APR-92	GENERAL CORRESP To FDA	OTHER	N/A	RESPONSE TO 14-APR-92 FDA TELEPHONE CALL RE: PRE-APPROVAL INSPECTIONS FOR JULY OF 1992
01-MAY-92	GENERAL CORRESP To FDA	CMC Dos Form/Potency:	DRUG PRODUCT	RESPONSE TO FDA REQUEST FOR INFORMATION
06-MAY-92	GENERAL CORRESP From FDA	CMC Dos Form/Potency:	DRUG PRODUCT	
	GENERAL CORRESP From FDA	CMC Dos Form/Potency:	DRUG SUBSTANCE	
12-MAY-92	GENERAL CORRESP To FDA	CLINICAL PRO#: INV NAME:	STUDY	RESPONSE TO FDA REQUEST FOR INFORMATION RE: STATISTICAL ANALYSIS
15-MAY-92	PHONE CALL	CMC Dos Form/Potency:	DRUG PRODUCT	FOLLOW-UP TO DISCUSSION ON CMC QUESTIONS

APPLICATION CHRONOLOGY REPORT

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Route of Admin.: SU Dosage Form: SOLUTION
Generic Name: enoxaparin 30 mg

COMM DATE	COMM TYPE	CONTENT Name/Description Details		Content Comments
20-MAY-92	PHONE CALL	OTHER	N/A	DISCUSS THE CMC, STABILITY AND REVIEW STATUS
02-JUN-92	PHONE CALL	CMC Dos Form/Potency: INJECTION	DRUG PRODUCT 30 mg	TO PROVIDE FDA'S STABILITY COMMITTEE' DECISION RE: TEMPERATURE AND TIME INTERVALS
11-JUN-92	PHONE CALL	OTHER	N/A	REVIEW STATUS UPDATE
16-JUN-92	GENERAL CORRESP From FDA	CMC Dos Form/Potency: INJECTION	DRUG PRODUCT	THREE REQUESTS RE: MICROBIOLOGICAL PORTION OF THE APPLICATION
17-JUN-92	PHONE CALL	CMC Dos Form/Potency: INJECTION	DRUG PRODUCT 30 mg	CONFERENCE CALL TO CLARIFY FDA REQUESTS FOR ADDITIONAL STABILITY INFO IN 06-MAY-92 LETTER
18-JUN-92	PHONE CALL	OTHER	N/A	FDA ADVISED EIAR DOES NOT FULLY MEET THE CRITERIA SPELLED OUT
19-JUN-92	AMENDMENT	CMC Dos Form/Potency: INJECTION	DRUG PRODUCT	RESPONSE TO 24-FEB-92 FDA LETTER PROVIDED REPRESENTATIVE TEST RESULTS & VALIDATION INFO
26-JUN-92	GENERAL CORRESP From FDA	OTHER	N/A	ACKNOWLEDGMENT OF RECEIPT OF 19-JUN-92 AND 24-FEB-92 AMENDMENTS. FDA EXTENEDED THE DUE DATE TO 26-OCT-92
29-JUN-92	AMENDMENT	CMC Dos Form/Potency:	DRUG PRODUCT	AMENDMENT TO A PENDING APPLICATION
	AMENDMENT	PHARMACOKINETICS	N/A	
14-JUL-92	PHONE CALL	OTHER	N/A	UPDATE OF APPLICATION STATUS FDA REQUESTED THAT WE SUBMIT SAFETY DATA UP TO AND INCLUDING 30-JUN-92
20-JUL-92	GENERAL CORRESP To FDA	CLINICAL PRO#: INV NAME:	STUDY	RESPONSE TO FDA REQUEST FOR CONFIRMATION THAT EX VIVO STUDIES ON ENO884 PATIENTS DID NOT JEOPARDIZE THE BLINDING

APPLICATION CHRONOLOGY REPORT

Run Date: 05/05/93
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Route of Admin.: SU Dosage Form: SOLUTION
Generic Name: enoxaparin 30 mg

COMM DATE	COMM TYPE	CONTENT Name/Description Details		Content Comments
23-JUL-92	PHONE CALL	LABEL/PRO MATERIAL FC NUM:	PACKAGE INSERT	TO ASCERTAIN FDA'S POSITION REGARDING LOVENOX PACKAGING
06-AUG-92	PHONE CALL	OTHER	N/A	REQUEST FOR STATISTICAL ANALYSIS
07-AUG-92	GENERAL CORRESP To FDA	OTHER	N/A	SELECTION OF LOVENOX AS THE TRADE NAME FOR MARKETING
11-AUG-92	GENERAL CORRESP To FDA	OTHER	N/A	PROVIDED CORRECTED VERSIONS OF APPENDICES XIV, XV AND XVI
13-AUG-92	GENERAL CORRESP To FDA	CMC Dos Form/Potency: INJECTION	DRUG PRODUCT	RESPONSE TO 16-JUN-92 FDA REQUEST FOR INFORMATION
07-OCT-92	PHONE CALL	CMC Dos Form/Potency:	DRUG PRODUCT	PROVIDED FDA WITH A STATUS UPDATE OF DR. TEMPLE'S REVIEW
10-NOV-92	FDA REPORT	SAFETY UPDATE	N/A	COVERING THE PERIOD 01-JAN-91 THROUGH 30-JUN-92
20-NOV-92	GENERAL CORRESP From FDA	LABEL/PRO MATERIAL FC NUM:	LABEL	PROVIDE DRAFT LABELING
23-NOV-92	GENERAL CORRESP To FDA	OTHER	N/A	RESPONSE TO APPROVALBE LETTER INTENT TO FILE AN AMENDMENT
24-NOV-92	GENERAL CORRESP To FDA	OTHER	N/A	RESPONSE TO 20-NOV-92 REQUEST FOR ENVIRONMENTAL ASSESSMENT
08-DEC-92	GENERAL CORRESP To FDA	LABEL/PRO MATERIAL FC NUM:	LABEL	RESPONSE TO 20-NOV-92 FDA REQUEST FOR INFORMATION
11-DEC-92	PHONE CALL	OTHER	N/A	FOLLOWUP TO OUR DRAFT LABELING SUBMISSION OF 08-DEC-92
17-DEC-92	GENERAL CORRESP To FDA	CMC Dos Form/Potency: INJECTION	DRUG PRODUCT 30 mg	RESPONSE TO FDA REQUEST FOR INFORMATION RE: STABILITY DATA FOR 30 MG PRODUCT
23-DEC-92	PHONE CALL	LABEL/PRO MATERIAL FC NUM:	PACKAGE INSERT	FDA REQUESTED REFERENCE TO ANTICOAGULANT ACTIVITY BE OMITTED FROM THE DESCRIPTION SECTION OF PI

APPLICATION CHRONOLOGY REPORT

Run Date: 05/05/93
App Num: 20164 Type: NDA Drug Code: RP 54563 Trade Name: LOVENOX INJECTION
Route of Admin.: SU Dosage Form: SOLUTION
Generic Name: enoxaparin 30 mg

COMM DATE	COMM TYPE	CONTENT Name/Description Details		Content Comments
24-DEC-92	GENERAL CORRESP To FDA	CMC Dos Form/Potency:	DRUG PRODUCT	RESPONSE TO 20-NOV-92 FDA LETTER
30-DEC-92	PHONE CALL	OTHER	N/A	STATUS REPORT OF NDA APPROVAL
08-JAN-93	GENERAL CORRESP To FDA	LABEL/PRO MATERIAL FC NUM:	OTHER	RESPONSE TO FDA REQUEST FOR INFORMATION RE: FINAL PRINTED LABELING
10-JAN-93	GENERAL CORRESP From FDA	CLINICAL PRO#: INV NAME:	STUDY	
14-JAN-93	GENERAL CORRESP From FDA	OTHER	N/A	AMENDMENT CONSIDERED MAJOR - FDA EXTENDED REVIEW DUE DATE TO 25-APR-93
19-JAN-93	GENERAL CORRESP To FDA	LABEL/PRO MATERIAL FC NUM:	OTHER	PROVIDED DRAFT INTRODUCTORY PROMOTIONAL INFORMATION
19-JAN-93	PHONE CALL	OTHER	N/A	TO DISCUSS THE STATUS OF OUR APPLICATION IN GENERAL
25-JAN-93	PHONE CALL	LABEL/PRO MATERIAL FC NUM:	OTHER	TO OBTAIN CLARIFICATION OF LABELING
27-JAN-93	PHONE CALL	LABEL/PRO MATERIAL FC NUM:	OTHER	TO DISCUSS THE INTRODUCTORY PROMOTIONAL LAUNCH CAMPAIGN MATERIAL
02-FEB-93	PHONE CALL	CMC Dos Form/Potency:	DRUG SUBSTANCE	NDA STATUS UPDATE
09-FEB-93	PHONE CALL	CMC Dos Form/Potency:	DRUG SUBSTANCE	RE: STATUS OF REVIEW
16-FEB-93	PHONE CALL	CLINICAL PRO#: INV NAME:	STUDY	TO REVIEW W/DR. VINCENT SLIGHT MODIFICATIONS TO PROTOCOL SUBMITTED 29-JAN-92
17-FEB-93	PHONE CALL	OTHER	N/A	NDA STATUS UPDATE
18-FEB-93	GENERAL CORRESP To FDA	CMC Dos Form/Potency:	DRUG PRODUCT	RESPONSE TO 15-JAN-93 REQUEST RE: CONTAMINATION TESTING OF DISTILLED WATER

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Route of Admin.: SU Dosage Form: SOLUTION
Generic Name: enoxaparin 30 mg

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23-FEB-93	GENERAL CORRESP To FDA	CMC Dos Form/Potency: INJECTION	DRUG PRODUCT	RESPONSE TO 15-JAN-93 FDA REQUEST FOR INFORMATION
10-MAR-93	GENERAL CORRESP From FDA	SAFETY UPDATE	N/A	FDA REQUESTS ADDITIONAL INFORMATION RE: 10-NOV-92 SAFETY UPDATE
29-MAR-93	GENERAL CORRESP From FDA	OTHER	N/A	APPROVAL LETTER
31-MAR-93	GENERAL CORRESP To FDA	LABEL/PRO MATERIAL FC NUM:	OTHER	PROVIDED AN ADDITIONAL PIECE FOR THE INTRODUCTORY PROMOTIONAL LAUNCH CAMPAIGN INFORMATION
09-APR-93	GENERAL CORRESP From FDA	LABEL/PRO MATERIAL FC NUM:	OTHER	FDA COMMENTS AFTER REVIEW OF INTRODUCTORY PROMOTIONAL MATERIALS

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Regulatory Affairs

APPLICATION CHRONOLOGY REPORT
Report Cover Page

Run Date: 05/05/93
User: ingres_prod

Selection Criteria

App Number: 31532

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Regulatory Affairs

APPLICATION CHRONOLOGY REPORT

Run Date: 05/05/93
App Num: 31532 Type: IND Drug Code: RP 54563 Trade Name: TO BE ASSIGNED
Route of Admin.: IV Dosage Form: INJECTION
Generic Name: enoxaparin 100 mg/mL

COMM DATE	COMM TYPE	CONTENT Name/Description Details		Content Comments
18-APR-88	ORIGINAL SUBMISSION	OTHER	N/A	ORIGINAL SUBMITTED
19-MAY-88	GENERAL CORRESP From FDA	OTHER	N/A	EFFECTIVE DATE OF IND
03-DEC-90	AMENDMENT	OTHER	N/A	PRE-NDA MEETING REQUEST
15-JAN-91	AMENDMENT	OTHER	N/A	REQUEST FOR PRE-NDA MEETING
17-JAN-91	AMENDMENT	OTHER	N/A	RPR NOTIFICATION OF TRANSFER OF OWNERSHIP OF IND TO RHONE-POULENC RORER 31-JUL-90
17-JAN-91	AMENDMENT	OTHER	N/A	RPP TRANSFER OF OWNERSHIP OF IND TO RHONE-POULENC RORER ON 31-JUL-90
06-FEB-91	GENERAL CORRESP From FDA	OTHER	N/A	FDA REQUEST FOR INFO TO COMPLETE THE CHANGE IN OWNERSHIP
01-MAR-91	AMENDMENT	OTHER	N/A	CONFIRMATION OF PRE-NDA MEETING & AGENDA
14-MAR-91	MEETING MINUTES	OTHER	N/A	PRE-NDA MEETING OVERVIEW
25-APR-91	AMENDMENT	CLINICAL PRO#: INV NAME:	STUDY	RESPONSE TO 21-AUG-89 FDA LETTER
	AMENDMENT	CMC Dos Form/Potency:	DRUG PRODUCT	RESPONSE TO 21-AUG-89 FDA LETTER
15-MAY-91	AMENDMENT	OTHER	N/A	RESPONSE TO 06-FEB-91 FDA LETTER RE: ADDITIONAL INFO ON TRANSFER OF OWNERSHIP
24-JUL-91	FDA REPORT	ANNUAL RPT	N/A	COVERING THE PERIOD 19-MAY-90 THROUGH 18-MAY-91
14-AUG-91	AMENDMENT	CLINICAL PRO#: INV NAME:	STUDY	RESPONSE TO 21-AUG-89 FDA LETTER
15-OCT-91	AMENDMENT	OTHER	N/A	CHANGE OF ADDRESS

APPLICATION CHRONOLOGY REPORT

Run Date: 05/05/93
App Num: 31532 Type: IND Drug Code: RP 54563 Trade Name: TO BE ASSIGNED
Route of Admin.: IV Dosage Form: INJECTION
Generic Name: enoxaparin 100 mg/mL

COMM DATE	COMM TYPE	CONTENT Name/Description Details	Content Comments
14-NOV-91	AMENDMENT	CLINICAL STUDY PRO#: 547 INV NAME: OVERDYKE,WILLIAM L RITTER,MERRILL	
21-NOV-91	AMENDMENT	CLINICAL STUDY PRO#: 547 INV NAME: COMP,PHILIP C	
22-NOV-91	AMENDMENT	CLINICAL STUDY PRO#: 547 INV NAME: GECKLER,RONALD W	
25-NOV-91	AMENDMENT	CLINICAL STUDY PRO#: 547 INV NAME: JOHNSON,GERHARD	
02-DEC-91	AMENDMENT	CLINICAL STUDY PRO#: 547 INV NAME: ZIMMERMAN,RICHARD	
09-DEC-91	AMENDMENT	CLINICAL STUDY PRO#: 547 INV NAME: FURMAN,W KIM	
11-DEC-91	AMENDMENT	CLINICAL STUDY PRO#: 547 INV NAME: KIM,HUGH C	
17-DEC-91	AMENDMENT	CLINICAL STUDY PRO#: 547 INV NAME: MATHEES,DONALD J	
06-JAN-92	AMENDMENT	CLINICAL STUDY PRO#: 547 INV NAME: BLAHA,J DAVID BONA,ROBERT D TROWBRIDGE,ARTHUR A	
08-JAN-92	AMENDMENT	CLINICAL STUDY PRO#: 547 INV NAME: WISE,GREGORY	

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Generic Name: enoxaparin 100 mg/mL

COMM DATE	COMM TYPE	CONTENT Name/Description Details	Content Comments
23-JUL-92	AMENDMENT	CLINICAL STUDY PRO#: 569 INV NAME: YOUNG,TIMOTHY	
23-JUL-92	AMENDMENT	CLINICAL STUDY PRO#: 569 INV NAME: MERLI,GENO J	
28-JUL-92	FDA REPORT	ANNUAL RPT N/A	COVERING THE PERIOD 19-MAY-91 THROUGH 18-MAY-92
12-AUG-92	AMENDMENT	CLINICAL STUDY PRO#: 569 INV NAME: TROWBRIDGE,ARTHUR A	
14-AUG-92	AMENDMENT	CLINICAL STUDY PRO#: 547 INV NAME: WINTERS,THOMAS F	
24-AUG-92	AMENDMENT	CLINICAL STUDY PRO#: 569 INV NAME: OVERDYKE,WILLIAM L	
26-AUG-92	AMENDMENT	CLINICAL STUDY PRO#: 569 INV NAME: JOHNSON,WILLIAM M	
02-SEP-92	AMENDMENT	CLINICAL STUDY PRO#: 569 INV NAME: TREMAINE,M DAVID	
08-SEP-92	AMENDMENT	CLINICAL STUDY PRO#: 547 INV NAME: MANNAL,RICHARD	
08-SEP-92	AMENDMENT	CLINICAL STUDY PRO#: 569 INV NAME: HAIRE,WILLIAM D	US00468 CARLTON SAVORY NOT IN SPIN
22-SEP-92	AMENDMENT	CLINICAL STUDY PRO#: 124 INV NAME: FURMAN,W KIM	

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COMM DATE	COMM TYPE	CONTENT Name/Description Details	Content Comments
15-JAN-92	AMENDMENT	CLINICAL STUDY PRO#: 547 INV NAME: GONZALES,FRANCISCO WHITSETT,THOMAS	
31-JAN-92	AMENDMENT	CLINICAL STUDY PRO#: 547 INV NAME: ALEDORT,LOUIS	
24-FEB-92	AMENDMENT	CLINICAL STUDY PRO#: 547 INV NAME: COMEROTA,ANTHONY J	
09-MAR-92	AMENDMENT	CLINICAL STUDY PRO#: 547 INV NAME: COLWELL,CLIFFORD	
10-MAR-92	AMENDMENT	CLINICAL STUDY PRO#: 547 INV NAME: BONA,ROBERT D	BURROUGHS, M.D.; SUSAN IS LISTED AS AN INVESTIGATOR BUT NOT IN SPIN 26-MAR-92
17-MAR-92	AMENDMENT	CLINICAL STUDY PRO#: 547 INV NAME: LYONS,ROGER M	
23-MAR-92	AMENDMENT	CLINICAL STUDY PRO#: 547 INV NAME: ECONOMIDES,NICHOLAS	
01-JUL-92	AMENDMENT	CLINICAL STUDY PRO#: 569 INV NAME: YOUNG,TIMOTHY	
02-JUL-92	AMENDMENT	CLINICAL STUDY PRO#: 127 INV NAME: SICA,DOMENIC A	GEHR, TODD W.B.; AND RIPLEY, ELIZABETH D. ARE CO-INVESTIGATORS
16-JUL-92	AMENDMENT	CLINICAL STUDY PRO#: 569 INV NAME: CHRISTIE,MICHAEL GUSTILO,RAMON O'DONNELL,DENIS M	

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07-OCT-92	AMENDMENT	CLINICAL	STUDY	
		PRO#: 569		
		INV NAME: STULBERG,BERNARD		
08-OCT-92	AMENDMENT	CLINICAL	STUDY	CO-INVESTIGATOR WILLIAM R. KENNEDY
		PRO#: 569		
		INV NAME: FURMAN,W KIM		
20-OCT-92	FDA REPORT	CLINICAL	STUDY	US00465 FITZGERALD, ROBERT H., NOT IN SPIN 10-NOV-92
		PRO#: 569		
		INV NAME: BERNASEK,THOMAS L		
11-NOV-92	AMENDMENT	CLINICAL	STUDY	CURTISS MULL IS NOT IN SPIN
		PRO#: 569		
		INV NAME:		
07-DEC-92	AMENDMENT	CLINICAL	STUDY	
		PRO#: 569		
		INV NAME: OHAR,JILL		
21-DEC-92	AMENDMENT	INVEST IND	N/A	EDWARDS, RICHARD L, THE SCHOOL OF MEDICINE OF THE UNIVERSITY OF CONNECTICUT, 263 FARMINGTON, FARMINGTON, CT 06030
12-JAN-93	AMENDMENT	CLINICAL	STUDY	
		PRO#: 569		
		INV NAME: FISHER,DAVID A		
19-JAN-93	AMENDMENT	CLINICAL	STUDY	
		PRO#: 569		
		INV NAME: WINTERS,THOMAS F		
26-JAN-93	AMENDMENT	CLINICAL	STUDY	
		PRO#: 569		
		INV NAME: GECKLER,RONALD W		
		RITTER,MERRILL		
11-FEB-93	AMENDMENT	CLINICAL	STUDY	
		PRO#: 569		
		INV NAME: LEDES,CLAUDE P		

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01-MAR-93	AMENDMENT	CLINICAL STUDY PRO#: 569 INV NAME: BERNASEK,THOMAS L WHITSETT,THOMAS	